

Claims

1. (Currently Amended) A method for classifying ~~a scenario~~ an unknown bioactive condition, comprising:

generating a scenario by exposing a biological system to two or more [[a]] bioactive condition conditions, including the unknown bioactive condition;

representing a response of the biological system, or portion thereof, to the bioactive condition conditions, where representing the response of the system comprises determining data sufficient to generate a feature space vector; and

attempting to classify a scenario by database comparison; and
outputting a classification result to a user.

2. (Original) The method according to claim 1 where the system comprises living cells.

3. (Withdrawn) The method according to claim 1 where the system comprises living organisms.

4. (Withdrawn) The method according to claim 1 where the system is a living organism.

5. (Withdrawn) The method according to claim 1 where the system is a microbial community.

6. (Withdrawn) The method according to claim 1 where the system is tissue.

7. (Currently Amended) The method according to claim 1 ~~where representing a response of the system comprises determining data sufficient to determine a numerical feature space vector, and the method further comprises comprising providing a database for comparison, the database being generated by exposing a biological system to known scenarios to determine a numerical feature space vector, and transforming the resulting feature space vector data.~~

8. (Currently Amended) The method according to claim 7 further comprising transforming the data by:

determining software expert parameters based on extracted numerical data, where experts encode functions that map the feature space vector to a set of scenarios; and weighting the expert parameters.

9. (Currently Amended) The method according to claim 7 where transforming the data comprises:

determining expert parameters based on extracted data, where experts encode functions that map the feature space vector to a set of scenarios;
~~weighting the expert parameters;~~ and
tuning the integrated expert.

10. (Currently Amended) The method according to claim 9 where tuning the integrated expert comprises adaptive expert calibration.

11. (Currently Amended) The method according to claim 7 where the known scenarios are simplex scenarios generated by exposing a single biological system serially to two or more bioactive conditions.

12. (Original) The method according to claim 1 where attempting to classify the bioactive condition by database comparison comprises:

exposing the system to one or more scenarios to provide sufficient data to generate a characteristic signature for the bioactive condition;
extracting data;
calculating a location of data clusters in feature space representing the characteristic signature of the bioactive condition;
comparing location of data clusters in feature space representing the characteristic signature of the bioactive condition relative to data clusters representing known bioactive conditions; and

determining a likelihood that a bioactive condition is a known bioactive condition.

13. (Currently Amended) The method according to claim 12 where calculating a relative location of data clusters is done with software experts, where experts encode functions that map the feature space vector to a set of scenarios.

14. (Original) The method according to claim 1 where attempting to classify the bioactive condition comprises:

exposing the system to one or more scenarios to provide sufficient data to generate a characteristic signature for the bioactive condition;

calculating a location of data clusters in feature space representing the characteristic signature of the bioactive condition;

comparing the location of data clusters representing the characteristic signature of the bioactive condition relative to data clusters representing known bioactive conditions; and

determining a likelihood that an unknown bioactive condition is a known bioactive condition.

15. (Currently Amended) The method according to claim 14 where calculating a relative location of data clusters is done with software experts, where experts encode functions that map the feature space vector to a set of scenarios.

16. (Currently Amended) The method according to claim 1 where attempting to classify a complex scenario comprises:

synthesizing a complex scenario from known scenarios present in the database, where exposing two or more biological systems serially to two or more bioactive conditions generates the complex scenario following mathematical transformation;

comparing the scenario generated by the bioactive condition to the complex scenario; and
determining a likelihood that a complex scenario is the scenario.

17. (Currently Amended) The method according to claim 16 where the known scenarios are simplex scenarios that are generated by exposing a single biological system serially to two or more bioactive conditions.

18. (Currently Amended) The method according to claim 17 where each simplex scenario is generated by applying an elicitor, where the elicitor comprises bioactive conditions and a protocol used to apply the bioactive conditions to one or more biological systems.

Claim 19 (Canceled).

20. (Currently Amended) The method according to claim ~~19~~ 18 where the ~~bioactive conditions have~~ elicitor has known effects on the system.

21. (Currently Amended) The method according to claim ~~19~~ 18 where the ~~bioactive conditions have~~ elicitor has unknown effects on the system.

22. (Original) The method according to claim 18 comprising repeatedly applying an unknown bioactive agent in combination with one or more elicitors.

Claims 23-27 (Canceled).

28. (Withdrawn) The method according to claim 7 where the system comprises living cells and the numerical feature space vector contains parameters selected from the group consisting of nucleic acid composition, membrane lipid fatty acid composition, metabolic activity, cellular secretions, chemical measurements, physical measurements, and combinations thereof.

29. (Withdrawn) The method according to claim 28 where nucleic acid composition is determined by 16S-RNA profiling.

30. (Withdrawn) The method according to claim 28 where membrane lipid fatty acid composition is determined by phospholipids fatty acid profiling.

31. (Withdrawn) The method according to claim 28 where metabolic activity is determined by community level physiological profiling.

32. (Withdrawn) The method according to claim 28 where chemical measurements are selected from the group consisting of organic pollutants, nutrient discharges, heavy metals, dissolved oxygen, pH, redox, chlorine ion concentration and combinations thereof.

33. (Withdrawn) The method according to claim 28 where physical measurements are selected from the group consisting of temperature, ultra-violet radiation intensity, light intensity, and combinations thereof.

34. (Withdrawn) The method according to claim 28 where physical measurement provides a measure of cell morphology and turbidity changes.

35. (Withdrawn) The methods according to claim 1 where the system comprises living cells and a numerical feature space vector contains measurements of changes in physical properties of semiconductor nanoparticles.

36. (Withdrawn) The method according to claim 1 where the system is a live cell, and a numerical feature space vector contains measurements of cellular processes selected from the group consisting of gene expression, cell regulation, metabolism, and combinations thereof.

37. (Withdrawn) The method according to claim 36 where changes in cellular processes are characterized using semiconductor nanoparticles.

38. (Withdrawn) The method according to claim 36 where gene expression is characterized using a technique selected from the group consisting of DNA microarray analysis,

recombinant marker analysis, green fluorescent protein analysis, enzymatic activity, semiconductor nanoparticle analysis, and combinations thereof.

39. (Withdrawn) The method according to claim 38 where the enzymatic activity is recombinant luciferase.

40. (Withdrawn) The method according to claim 38 where analyzing gene expression comprises detecting protein expression using immunodetection.

41. (Withdrawn) The method according to claim 40 where immunodetection comprises western blotting, lateral flow immunodetection, immune precipitation, and combinations thereof.

42. (Withdrawn) The method according to claim 38 where cell regulation is characterized using changes in protein phosphorylation patterns.

43. (Withdrawn) The method according to claim 42 where changes in protein phosphorylation patterns are measured using 2-D gel electrophoresis.

44. (Withdrawn) The method according to claim 38 where cell regulation is characterized through changes in gene expression patterns characterized using DNA microarray analysis.

45. (Withdrawn) The method according to claim 38 where changes in cellular processes are determined by measuring growth medium composition.

46. (Withdrawn) The method according to claim 38 where changes in cellular processes are determined by measuring metabolite secretion patterns.

47. (Withdrawn) The method according to claim 38 where changes in cellular processes are determined by measuring protein secretion patterns.

48. (Withdrawn) The method according to claim 40 where measurements are made using methods selected from the group consisting of gas chromatography, liquid chromatography, mass spectrometry, nuclear magnetic resonance spectrometry, gel electrophoresis, and combinations thereof.

49. (Withdrawn) The method according to claim 38 where changes in cell metabolism are determined by intracellular measurements of metabolite levels.

50. (Withdrawn) The method according to claim 49 where intracellular measurements are made using metabolite secretion patterns provided by gas chromatography, liquid chromatography, mass spectrometry, nuclear magnetic resonance spectrometry, and combinations thereof.

51. (Withdrawn) The method according to claim 1 where the system is a live chromatophore.

52. (Withdrawn) The method according to claim 51 where the chromatophore is a fish chromatophore.

53. (Withdrawn) The method according to claim 52 where the fish chromatophore is a *Betta* chromatophore.

54. (Withdrawn) The method according to claim 51 where the chromatophore is a frog chromatophore.

55. (Withdrawn) The method according to claim 54 where the frog chromatophore is a *Xenopus* chromatophore.

56. (Withdrawn) The method according to claim 2 where the living cells are immortalized.

57. (Withdrawn) The method according to claim 56 where the living cells are frog chromatophores.

58. (Withdrawn) The method according to claim 7 where the living system is a chromatophore and the numerical feature space vector includes color change measurements.

59. (Withdrawn) The method according to claim 58 where the measurements are of changes in the refracted wavelength of light, color intensity, cell morphology, cell area, cell motility or any combination thereof.

60. (Withdrawn) The method according to claim 58 where color change measurements are made by:

- acquiring images of the chromatophore, such images reflecting response of the chromatophore to a scenario;

- converting response changes to hue, saturation, value histograms;

- applying probabilistic segmentation to assign a probability that a histogram data point belongs to a particular group of data points in the histogram to isolate data points representing response of the chromatophore to the scenario from extraneous information, thereby providing probabilistic clusters for chromatophore responses of interest for segmenting each of the images into image classes;

- dividing the images into plural subfields;

- extracting numerical information for each subfield from the image segments, such numerical information representing features of the images having information concerning the chromatophore response to the scenario;

- generating numerical data for each subfield for each chromatophore response monitored;

- applying a model fitting procedure to the set of numerical data and identifying model parameters; and

- using at least a portion of the model parameters to define a feature model space having scenario clusters for known materials.

61. (Withdrawn) The method according to claim 51 where exposing the chromatophore to a known scenario comprises providing an apparatus comprising a digital camera for recording images, a receiver for receiving live cells, an injection port for injecting a material into contact with the chromatophore, and a computer for processing information concerning response of the chromatophore to the material.

62. (Withdrawn) The method according to claim 1 where the system comprises a live cell, and the method comprises:

- exposing the live cell to a scenario;
- imaging the live cell to provide images of cellular response to the scenario;
- repeating steps as necessary for providing sufficient data for possibly classifying the scenario; and
- attempting to classify the scenario by database comparison to known scenarios using software experts.

63. (Withdrawn) The method according to claim 62 where the system comprises plural live cells.

64. (Withdrawn) The method according to claim 62 where no information concerning the scenario is included in the database information.

65. (Withdrawn) The method according to claim 63 where the known scenario is a complex scenario.

66. (Withdrawn) The method according to claim 65 where the complex scenario comprises multiple simplex scenarios.

67. (Withdrawn) The method according to claim 63 where each simplex scenario is an elicitor.

68. (Withdrawn) The method according to claim 67 where the elicitor consists of a known bioactive condition and the protocol utilized to apply the bioactive conditions to the system.

69. (Withdrawn) The method according to claim 68 where the bioactive condition has known effects on biological pathways.

70. (Withdrawn) The method according to claim 68 where the bioactive conditions have unknown effects on biological pathways.

71. (Withdrawn) The method according to claim 70 where the biological pathways are cell signaling pathways that control cell function.

72. (Withdrawn) The method according to claim 55 where each repeated step consists of application of an unknown bioactive agent in combination with one or more elicitors.

73. (Withdrawn) The method according to claim 62 where the complex scenario comprises simplex scenarios that represent information regarding the mechanism of action of known bioactive conditions.

74. (Withdrawn) The method according to claim 62 where classifying the scenario with respect to the complex scenario provides information about mechanism of action of the bioactive condition.

75. (Withdrawn) The method according to claim 62 where classification involves determining the likelihood that the scenario is a known scenario.

76. (Withdrawn) The method according to claim 62 where the system comprises plural live cells and database information is obtained by:

serially exposing plural live cells to a known scenario;

acquiring images of the cells reflecting response of the cells to the scenario;

converting response changes to hue, saturation, value histograms;
applying probabilistic segmentation to assign a probability that a histogram data point belongs to a particular group of data points in the histogram to isolate data points representing response of the cells to the scenario from extraneous information, thereby providing probabilistic clusters for cell responses of interest for segmenting each of the images into image classes;
dividing the images into plural subfields;
extracting numerical data sets for each subfield from the image segments, such numerical information representing features of the images having information concerning the cellular response to the scenario;
applying a model fitting procedure to each data set and extracting corresponding model parameters; and
using at least a portion of the model parameters to define a feature model space having scenario clusters for known materials.

77. (Withdrawn) The method according to claim 76 where attempting to classify the scenario comprises:

repeatedly exposing the cells to an unknown scenario, and repeating steps required for providing a model space having statistical expert information concerning the unknown scenario;
calculating distances between clusters representing unknown scenarios and known scenarios; and
determining a likelihood that an unknown scenario is a known scenario by combining such distances by expert voting.

Claim 78 (Canceled).

79. (Withdrawn) The method according to claim 49 where feature space dimensionality is controlled by elicitor set size.

80. (Original) The method according to claim 1 useful for classifying unknown drug candidates.

81. (Original) The method according to claim 1 useful for classifying unknown toxins.

82. (Original) The method according to claim 81, comprising:
identifying cell type and cell response most useful for providing information concerning cellular response to a particular scenario;
generating a database of scenarios; and
classifying unknowns by comparison with numerical feature space vector created by known scenarios.

83. (Original) The method according to claim 1 the system comprises non-pigmented cells.

84. (Withdrawn) The method according to claim 76 where exposing comprises using an apparatus comprising a digital camera for recording images, a receiver for receiving live cells, an injection port for injecting a material into contact with the cells, and a computer for processing information concerning response of the cells to the material.

85. (Withdrawn) The method according to claim 84 where the apparatus comprises plural cameras.

86. (Withdrawn) The method according to claim 85 where the scenario comprises exposing the cells to a chemical or biological agent.

87. (Withdrawn) The method according to claim 86 where the scenario comprises a chemical agent, and the cells are exposed to the chemical agent at varying concentrations.

88. (Withdrawn) The method according to claim 87 where the data-fitting model is a parametric nonlinear dynamic model.

89. (Withdrawn) The method according to claim 84 where the model parameter represents a single cell response.

90. (Withdrawn) The method according to claim 84 where the model parameter represents plural cell responses.

91. (Withdrawn) The method according to claim 85 where the model parameters are time dependent.

92. (Withdrawn) The method according to claim 84 where the model parameters are time independent.

93. (Withdrawn) The method according to claim 84 where the expert parameter represents a cellular state prior to exposure to the material and subsequent to exposure to the material.

94. (Withdrawn) The method according to claim 84 where determining a probability that the unknown scenario is a known scenario comprises determining a Mahalanobis distance for the unknown scenario relative to at least one known scenario cell reaction model space.

95-107. (Canceled)

108. (Original) A computer program encoding the method of claim 1.

109. (Original) A computer programmed with the computer program of claim 108.

110. (Original) A computer-readable medium on which is stored a computer program having instructions for executing the method of claim 1.

111. (Withdrawn) The method according to claim 1 where the system is a living cell that experiences a detectable change in response to an interaction with a bioactive condition.

112. (Withdrawn) The method according to claim 11 where the living cell is selected from the group consisting of a PC12 pheochromocytoma cell, a *HeLa* cell, and combinations thereof.

113. (Withdrawn) The method according to claim 111 where the living cells are cancer cells.

114. (Withdrawn) The method according to claim 113 where the living cells are selected from the group consisting of *HeLa* cells, 3T3 cells, COS7 cells, HEPG2 cells, and combinations thereof.

115. (Original) The method according to claim 2 where the change detected in the living cells is cytoplasmic streaming.

116. (Withdrawn) The method according to claim 1 where the system is a mammal.

117. (Withdrawn) The method according to claim 1 where the system is a fish.

118. (New) The method according to claim 1 where generating a scenario comprises exposing a biological system to two or more bioactive conditions consecutively.

119. (New) The method according to claim 1 where the feature space vector has both numerical and non-numerical feature descriptors.